

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please replace the paragraph on page 5, lines 8-17 as follows:

-- In this setting, there is great concern about the possible ~~emerge~~ emergence of methicillin-resistant/multi-drug resistant *S. aureus* strains which are vancomycin resistant – and which would be essentially untreatable. Although overt resistance to vancomycin has not yet been documented in clinical isolates, there have been several reports of clinical infections with *S. aureus* strains having intermediate resistance to vancomycin (MICs = 8 µg/ml), which suggests that untreatable staphylococcal infections may not be too far away [Tenover, F. C., and R. P. Gaynes. 2000]. Given the virulence of *S. aureus*, the emergence of such untreatable strains would be devastating and have a major impact on the way in which medicine is practiced in this country.--

Please replace the paragraphs on page 6, lines 4-17 as follows:

--*Pseudomonas aeruginosa* is a highly virulent gram-negative bacterial species that is responsible for bacteremia, wound infections, pneumonia, and urinary tract infections. Increasing problems with multi-antibiotic resistance in *Pseudomonas* has been noted in hospitals, with particular concern focusing on strains which are generally designated as “Imipenem-resistant *Pseudomonas*”, reflecting the last major antimicrobial agent to which they have become resistant. Many of these strains are resistant to all major antibiotic classes, presenting substantive difficulties in management of infected patients.

As seen with other Gram-negative microorganisms, *Pseudomonas* strains often emerge as the primary colonizing flora of the posterior pharynx during hospitalization. Strains present in the posterior pharynx, in turn, are more likely to be aspirated into the lungs, and cause pneumonia. In this setting, colonization with multi-drug resistant *Pseudomonas* represents a potentially serious risk factor for development of multi-drug resistant *Pseudomonas* pneumonia.--

Please replace the paragraph on page 10, lines 10-19 as follows:

--Infections treated with bacteriophage included osteomyelitis, sepsis, empyema, gastroenteritis, suppurative wound infection, pneumonia and dermatitis. Pathogens involved included *Staphylococci*, ~~*Streptococci*~~ *Streptococci*, *Klebsiella*, *Shigella*, *Salmonella*, *Pseudomonas*, *Proteus* and *Escherichia*. These articles reported a range of success rates for phage therapy between ~~80-95%~~ 80-

95% with only rare reversible allergic or gastrointestinal side effects. These results indicate that bacteriophage may be a useful adjunct in the fight against bacterial diseases. However, this literature does not describe, in any way anticipate, or otherwise suggest the use of bacteriophage to modify the composition of colonizing bacterial flora in humans, thereby reducing the risk of subsequent development of active infections.--

Please replace the paragraph on page 18, lines 21-27 as follows:

--Quantities of broad-spectrum VRE-active bacteriophage needed for therapeutic uses described below may be produced by culture on a suitable host strain in the ~~mariner~~ manner described above for enrichment culture. When performing an enrichment culture to produce bacteriophage for therapeutic use, a host strain is selected based on its ability to give a maximum yield of phage, as determined in pilot experiments with several different host VRE strains. If two or more host strains give similar yield[[?]], the strain most sensitive to antibiotics is selected.--

Please replace the paragraph on page 21, lines 18-31 as follows:

--Dose and duration of therapy will depend on a variety of factors, including the patient age, patient weight, and tolerance of the ~~page~~ phage. Bacteriophage may be administered to patients in need of the therapy provided by this invention by oral administration. Based on previous human experience in Europe, a dose of phage between 10^7 and 10^{11} PFU will be suitable in most instances. The phage may be administered orally in, for example, mineral water, optionally with 2.0 grams of sodium bicarbonate added to reduce stomach acidity. Alternatively, sodium bicarbonate may be administered separately to the patient just prior to dosing with the phage. Phages also may be incorporated in a tablet or capsule which will enable transfer of phages through the stomach with no reduction of phage viability due to gastric acidity, and release of fully active phages in the small intestine. The frequency of dosing will vary depending on how well the phage is tolerated by the patient and how effective a single versus multiple dose is at reducing VRE gastrointestinal colonization.--

Please replace the paragraph on page 22, lines 1-7 as follows:

--The dose of VRE-active bacteriophage and duration of therapy for a particular patient can be determined by the skilled clinician using standard pharmacological approaches in view of the above factors. The response to treatment may be monitored by, analysis of blood or body fluid

levels of VRE, or VRE levels in relevant tissues or monitoring disease state in the patient. The skilled clinician will adjust the dose and duration of therapy based ~~on~~ on the response to treatment revealed by these measurements.--

Please replace the paragraph on page 23, lines 1-31 as follows:

--In the 1980's a number of British studies were conducted which demonstrated the efficacy of bacteriophage prophylaxis and therapy in mice and farm animal models. These studies were significant because the titers of the phage preparations administered were significantly less than the bacterial inoculum indicating in vivo bacteriophage multiplication. For example, Smith et al (Smith, et al. (1982), "Successful treatment of experimental *Escherichia coli* infections in mice using phage: its general superiority over antibiotics." *J. Gen. Microbiol.*, 128:307-1825) found intra-muscular inoculation of mice with 10^6 CFU of *E. coli* with K1 capsule killed 10/10 mice. However when mice were simultaneously intramuscularly inoculated with 10^4 PFU of phage, at a separate site, 10/10 mice survived. Smith and coworkers demonstrated that administration of a mixture of two phage resulted in high levels of protection of calves with diarrhea induced by *E. coli* with K 88 or K99 fimbriae (Smith, et al. (1983), "Effectiveness of phages in treating experimental *Escherichia coli* diarrhea in calves, piglets and lambs." *J. Gen. Microbiol.*, 129:2659-75; Smith, et al. (1987), "The control of experimental *Escherichia coli* diarrhea in calves by means of bacteriophage." *J. Gen. Microbiol.*, 133:1111-26; Smith, et al. (1987), "Factors influencing the survival and multiplication of bacteriophages in calves and in their environment." *J. Gen. Microbiol.*, 133:1127-35). If the phage was administered before or at ~~the~~ the same time as *E. coli* no deaths occurred and complete protection was attained. Control animals developed watery diarrhea and died within 2 to 5 days. If phage administration was delayed until the onset of diarrhea, protection was not complete although the severity of infection was greatly reduced and no deaths were observed. Berchieri, et al., found that fewer chicks orally infected with 10^9 PFU of *Salmonella typhimurium* died when 10^9 PFU of *Salmonella* specific phage was orally administered soon after initiation of the bacterial infection (Berchieri, et al. (1991), "The activity in the chicken alimentary tract of bacteriophages lytic for *Salmonella typhimurium*." *Res. Microbiol.*, 142:541-49). They also found that the phage was readily spread between the different infected birds.--

Please replace the paragraph at on page 33, line 29 to page 34, line 5 as follows:

--For purposes of ~~clarity~~ clarity of understanding, the foregoing invention has been described in some detail by way of illustration and example in conjunction with specific embodiments, although other aspects, advantages and modifications will be apparent to those skilled in the art to which the invention pertains. The foregoing description and examples are intended to illustrate, but not limit the scope of the invention. Modifications of the above-described modes for carrying out the invention that are apparent to persons of skill in medicine, bacteriology, infectious diseases, pharmacology, and/or related fields are intended to be within the scope of the invention, which is limited only by the appended claims.--